Office Action Summary	Application No.	Applicant(s)
	10/559,596	SPIES ET AL.
	Examiner	Art Unit
	Jennifer Dunston	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3 June 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,11,12 and 14-25* is/are pending in the application.

4a) Of the above claim(s) *16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-8, 11, 12, 14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 6/3/2011, in which claims 4, 5, 9, 10 and 13 were canceled, and claims 1, 8 and 11 were amended. Claims 1-3, 6-8, 11, 12 and 14-25 are pending in the instant application.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicants elected Group I without traverse in the reply filed on 7/9/2010.

Claims 16-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/9/2010.

Claims 1-3, 6-8, 11, 12, 14 and 15 are under consideration.

Response to Arguments - Claim Objections

The objection of claims 4, 5, 9, 10 and 13 is moot in view of Applicant's cancellation of the claims.

The objection of claims 6, 11 and 14 has been withdrawn in view of Applicant's amendment to the claims. Specifically, claim 1 was amended to recite "wherein the expression cassette comprises nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3," and the claims further limit this sequence.

Response to Arguments - 35 USC § 101

The rejection of claims 8-14 under 35 USC § 101 has been withdrawn in view of Applicant's amendment to the claims in the reply filed 6/3/2011.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-8, 11, 12, 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new rejection, necessitated by the amendment of claim 1 in the reply filed 6/3/2011.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "an expression cassette comprising from 5' to 3' the following elements: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence, wherein the expression cassette comprises nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3" are unclear. The phrase is unclear in that it sets forth two definitions of the claimed expression cassette which are not consistent with one another. The expression cassette is first defined as comprising from 5' to 3' the following elements: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and

a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence. The expression cassette is then defined as comprising nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3. However, nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 do not contain all of the elements recited in the first definition of the expression cassette and do not contain the elements in the required order of the first definition. Specifically, the specification discloses that SEQ ID NO: 3 contains the following regions: (i) a first region (bases 1-1368 of SEQ ID NO: 3), which contains the viral promoter, enhancer and intron A, corresponding to bases 512-1513 and 1736-2094 of the major-immediate early gene of CMV (GenBank Accession No. M60321); (ii) a second region (bases 1369-1416 of SEQ ID NO: 3), which contains recognition sites for 6 restriction enzymes and was derived from annealed oligonucleotides, where this region allows for cloning of a gene (heterologous sequence) into the vector; and (iii) a third region (bases 1417-1651 of SEQ ID NO: 3), which contains the early and late polyadenylation signals of the SV40 virus and provides the necessary polyA sites for the mRNA transcript of a gene that is later cloned into the second region (e.g., Example 1 of the specification). GenBank Accession No. M60321 (cited in a prior action) shows that nucleotides 534-1081 contain the CMV enhancer, nucleotides 1082-1120 contain the promoter, and nucleotides 1265-2088 contain intron A (the first intron). Thus, nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 contain from 5' to 3' the following elements: a CMV enhancer, a CMV promoter, a CMV intron A sequence from the CMV major immediate early gene, a multiple cloning site, and a polyadenylation site. Accordingly, the two definitions of the expression cassette provided in claim 1 are inconsistent with one another. Furthermore, the specification defines the term "operably linked" to mean DNA regions that are functionally

related to each other, and states, "a promoter is 'operably linked' to a coding sequence if it controls the transcription of the sequence." See page 22, paragraph [0075]. The claim first defines the expression cassette as comprising a promoter and heterologous nucleic acid sequence, "wherein the promoter is operably linked to the heterologous nucleic acid sequence." Given the definition of "operably linked" provided in the specification and the dependent claims that limit the heterologous sequence to a cancer antigen (claim 3), such as the cancer antigen encoded by the nucleotide sequence set forth in SEQ ID NO: 6 (claim 7), the claim is reasonably interpreted as requiring a heterologous protein coding sequence to be linked to the promoter so that the promoter is capable of controlling the expression of the protein coding sequence. However, nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 do not contain a heterologous sequence. The specification clearly teaches that SEQ ID NO: 3 contains recognition sites for 6 restriction enzymes, which are to be used to clone in a heterologous sequence (e.g., Example 1). The heterologous sequence is not present in the sequence of nucleotides 1-1653 of SEQ ID NO: 3. It would be remedial to separately claim these two embodiments in different independent claims. For example, one independent claim should be directed to an expression vector comprising an expression cassette comprising from 5' to 3' the following elements: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence. A second independent claim should be drawn to an expression vector comprising nucleotides 1-1653 of the sequence of SEQ ID NO: 3.

Claims 2, 3, 6-8, 11, 12, 14 and 15 depend from claim 1 and are rejected for the same reasons applied to claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-8, 11, 12, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (A) an expression vector comprising the sequence of SEQ ID NO: 3; (B) an expression vector comprising nucleotides 1-1653 of the sequence of SEQ ID NO: 3; and (C) an expression vector comprising an expression cassette comprising from 5' to 3' the following elements: a CMV enhancer sequence, a CMV promoter sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence, does not reasonably provide enablement for making an expression vector comprising from 5' to 3' the following elements: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence, where the sequence of nucleotides 1-1653 of SEQ ID NO: 3 is used to provide each of these elements in the required order. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a new rejection, necessitated by the amendment of claim 1 in the reply filed 6/3/2011.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims require "an expression cassette comprising from 5' to 3' the following elements: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence, wherein the expression cassette comprises nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3." The nature of the invention is complex in that it provides two definitions of the claimed expression cassette which are not consistent with one another. The expression cassette is first defined as comprising from 5' to 3' the following elements: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence. The expression cassette is then defined as comprising nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3. However, nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 do not contain all of the elements recited in the first definition of the expression cassette and do not contain the elements in the required order of the first definition.

Breadth of the claims: The claims are narrow in that the specifically require nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 to provide the following elements in a 5' to 3'

order: a CMV promoter sequence, a CMV enhancer sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence. The narrowness of the claims is a problem, because the claimed elements are not all present in the required order within nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3.

Guidance of the specification and existence of working examples: the specification discloses that SEQ ID NO: 3 contains the following regions: (i) a first region (bases 1-1368 of SEQ ID NO: 3), which contains the viral promoter, enhancer and intron A, corresponding to bases 512-1513 and 1736-2094 of the major-immediate early gene of CMV (GenBank Accession No. M60321); (ii) a second region (bases 1369-1416 of SEQ ID NO: 3), which contains recognition sites for 6 restriction enzymes and was derived from annealed oligonucleotides, where this region allows for cloning of a gene (heterologous sequence) into the vector; and (iii) a third region (bases 1417-1651 of SEQ ID NO: 3), which contains the early and late polyadenylation signals of the SV40 virus and provides the necessary polyA sites for the mRNA transcript of a gene that is later cloned into the second region (e.g., Example 1 of the specification).

Furthermore, the specification defines the term "operably linked" to mean DNA regions that are functionally related to each other, and states, "a promoter is 'operably linked' to a coding sequence if it controls the transcription of the sequence." See page 22, paragraph [0075]. The claim first defines the expression cassette as comprising a promoter and heterologous nucleic acid sequence, "wherein the promoter is operably linked to the heterologous nucleic acid

sequence." Given the definition of "operably linked" provided in the specification and the dependent claims that limit the heterologous sequence to a cancer antigen (claim 3), such as the cancer antigen encoded by the nucleotide sequence set forth in SEQ ID NO: 6 (claim 7), the claim is reasonably interpreted as requiring a heterologous protein coding sequence to be linked to the promoter so that the promoter is capable of controlling the expression of the protein coding sequence. However, nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 do not contain a heterologous sequence. The specification clearly teaches that SEQ ID NO: 3 contains recognition sites for 6 restriction enzymes, which are to be used to clone in a heterologous sequence (e.g., Example 1). The heterologous sequence is not present in the sequence of nucleotides 1-1653 of SEQ ID NO: 3.

Predictability and state of the art: GenBank Accession No. M60321 (cited in a prior action) shows that nucleotides 534-1081 contain the CMV enhancer, nucleotides 1082-1120 contain the promoter, and nucleotides 1265-2088 contain intron A (the first intron). Based upon the teachings of the specification and prior art, nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3 contain from 5' to 3' the following elements: a CMV enhancer, a CMV promoter, a CMV intron A sequence from the CMV major immediate early gene, a multiple cloning site, and a polyadenylation site. One would not have been able to use nucleotides 1-1653 of SEQ ID NO: 3 as an expression cassette containing from 5' to 3' the following elements: a CMV enhancer, a CMV promoter, a CMV intron A sequence from the CMV major immediate early gene, a multiple cloning site, and a polyadenylation site, because those elements are not present in that arrangement.

Amount of experimentation necessary: One would not have been able to use nucleotides 1-1653 of SEQ ID NO: 3 as an expression cassette containing from 5' to 3' the following elements: a CMV enhancer, a CMV promoter, a CMV intron A sequence from the CMV major immediate early gene, a multiple cloning site, and a polyadenylation site, because those elements are not present in that arrangement. No amount of experimentation would allow one to produce the claimed expression cassette. Based upon the teachings of the specification and prior art, the skilled artisan would have to choose to make a vector that contained (1) from 5' to 3' the following elements a CMV enhancer sequence, a CMV promoter sequence, a CMV intron A sequence from the CMV major immediate early gene, a heterologous nucleic acid sequence, and a polyadenylation site, wherein the promoter is operably linked to the heterologous nucleic acid sequence; or (2) nucleotides 1-1653 of SEQ ID NO: 3.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-3, 6-8, 11, 12, 14 and 15 are not considered to be enabled by the instant specification.

Response to Arguments - 35 USC § 112

The rejection of claims 4, 9 and 13 under 35 U.S.C. 112, second paragraph, is moot in view of Applicant's cancellation of the claims in the reply filed 6/3/2011.

The rejection of claims 4, 9 and 13 under 35 U.S.C. 112, first paragraph (written description), is moot in view of Applicant's cancellation of the claims in the reply filed 6/3/2011.

The rejection of claims 4, 9 and 13 under 35 U.S.C. 112, first paragraph (enablement), is moot in view of Applicant's cancellation of the claims in the reply filed 6/3/2011.

Response to Arguments - 35 USC § 102

The rejection of claims 1-3, 8, 12 and 15 under 35 U.S.C. 102(e) as being anticipated by Thudium et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 6/3/2011. Thudium et al do not teach nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3, which is required by the claims.

Response to Arguments - 35 USC § 103

The rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Thudium et al in view of Wang has been withdrawn in view of Applicant's amendment to the claims in the reply filed 6/3/2011. The cited references do not teach nucleotides 1-1653 of the sequence set forth in SEQ ID NO: 3, which is required by the claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is (571)272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Dunston/
Primary Examiner
Art Unit 1636